Armed Forces College of Medicine

AFCM

Nutritionally essential vitamins 1

(B2, B3 & B6)

By

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INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1. **Distinguish the active forms and functions of vitamins (B2, B3 & B6)**
2. **Correlate vitamins (B2, B3 & B6) deficiencies to their clinical disorders**

Contents:

Riboflavin (vitamin B2)

Niacin (nicotinic acid) (vitamin B3)

Pyridoxine (vitamin B6)

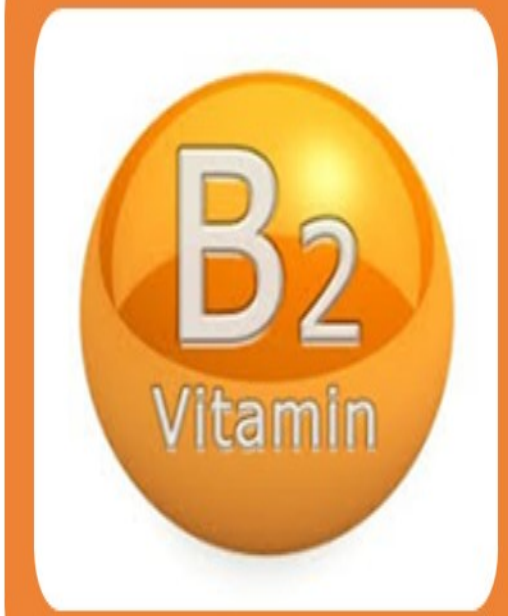
Vitamins

1. Vitamins are **organic nutrients** that are required to **small quantities** for a variety of biochemical functions.

2. They **cannot be synthesized** by the body in adequate amounts and must therefore be supplied i

3. They are **necessary to maintain good healt**

4. Absence or relative **deficiency** of vitamins in diet leads to characteristic deficiency states and **diseases**.

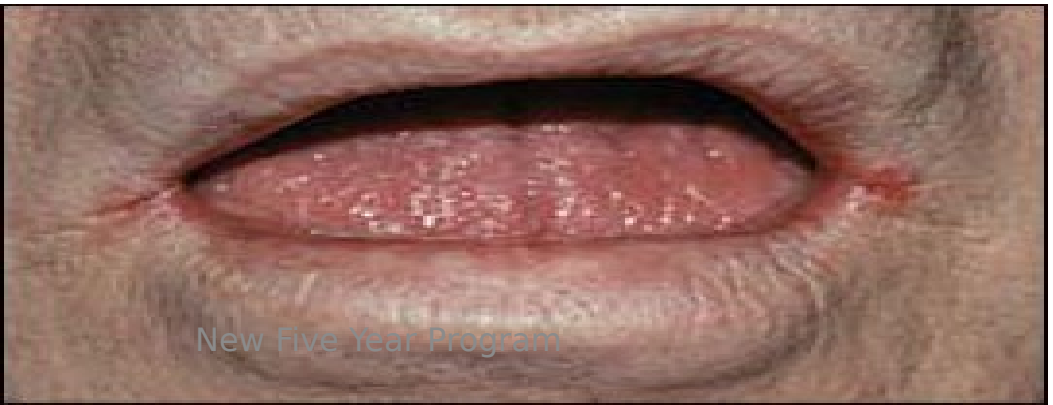


Riboflavin (vitamin B2)

Case scenario

A male patient on prolonged intravenous fluid complaining of red painful angle of the mouth, swollen fissured lips , sandy sensation and red coloration of eye. Urine analysis revealed low levels of Riboflavin vitamin (B2)

1- What is the suspected diagnosis?



Functions of Riboflavin vitamin (B2)

Active forms: flavin adenine dinucleotide (FAD) a

flavin mononucleotide (FMN) which acts as hydrogen carrier *in oxidation-reduction* reactions

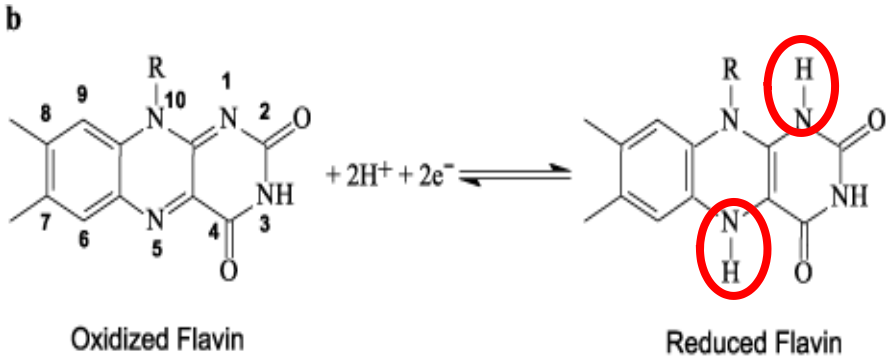
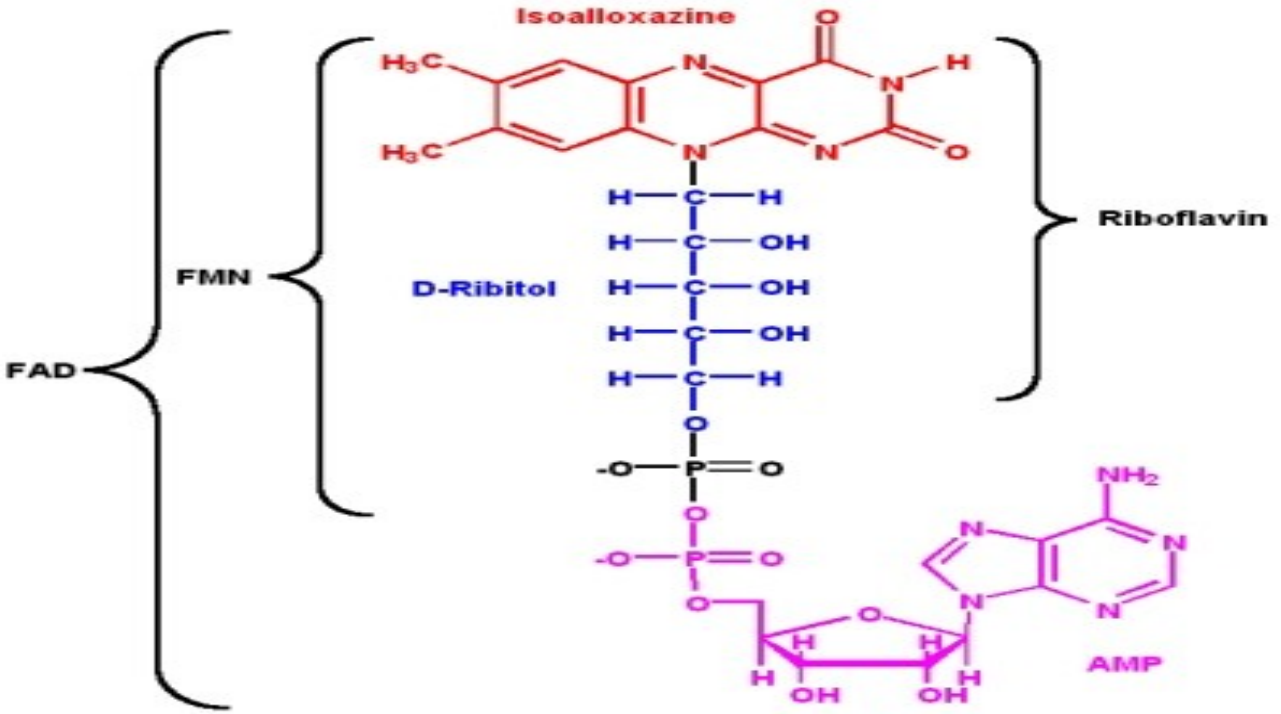
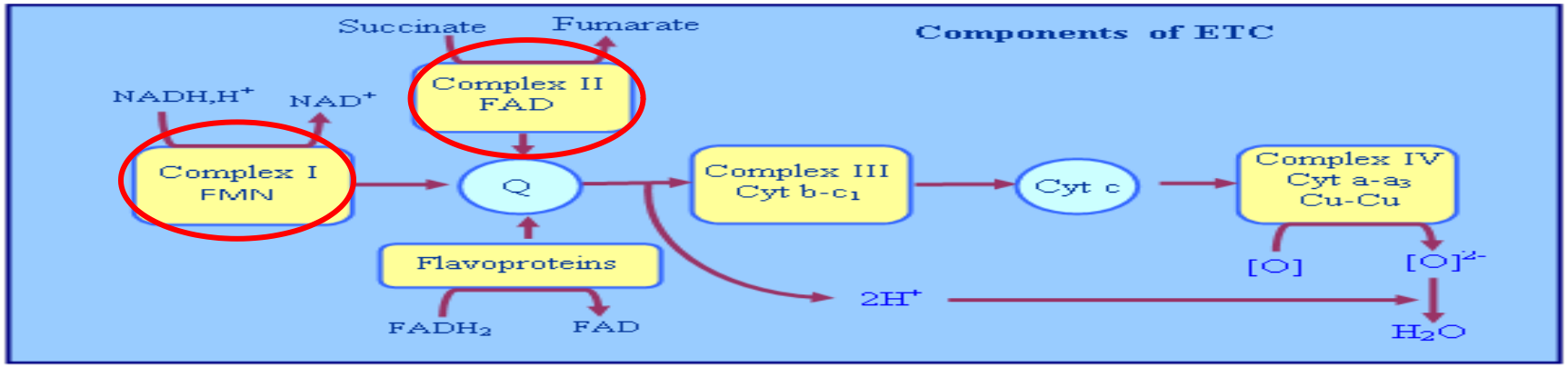


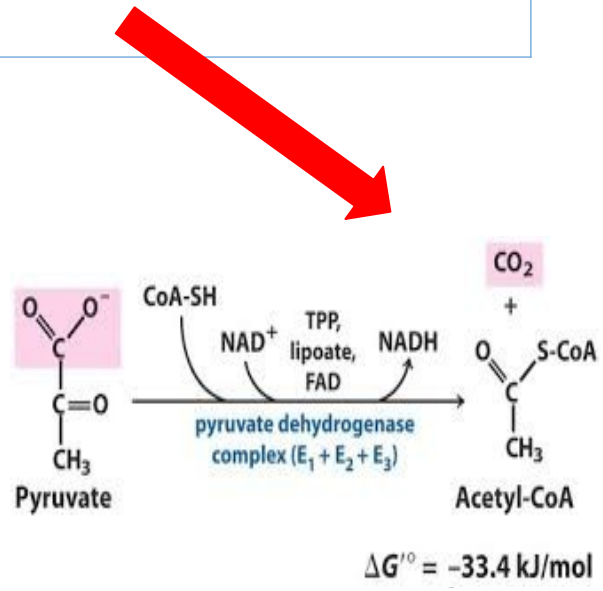
Figure 1. Chemical structures and nomenclature of the flavins in the oxidized state (a) and redox process of part (alloxazin ring) of the flavin structure (b).



Functions of Riboflavin vitamin (B2)

Reactions catalyzed by FAD	Reactions catalyzed by FMN
Succinate dehydrogenase -1 (complex ll in the ETC)	NADH dehydrogenase (complex -1 l in the ETC)
Glycine oxidase -2	L-amino acid oxidase -2
Alpha keto acids -3 dehydrogenase complex	

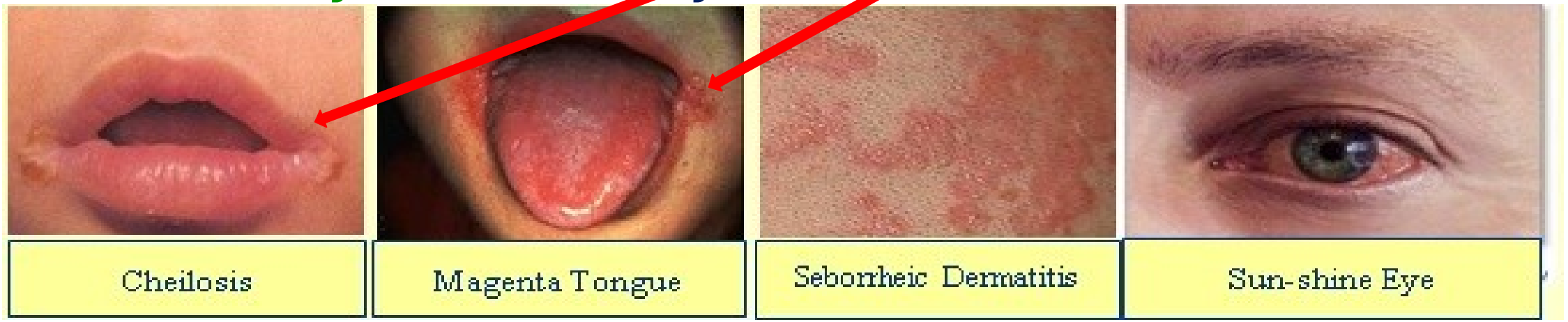




Deficiency Manifestations of B2

Affects mainly skin and mucous membranes

1. **Cheilosis** (swollen, fissured and congested lips)
2. **Angular stomatitis** (inflammation and fissures at the angles of the mouth)
3. **Glossitis** (magenta tongue)
4. **seborrheic dermatitis**,
5. **sun-shine eyes** due to conjunctivitis.



FAD and FMN are the active forms of

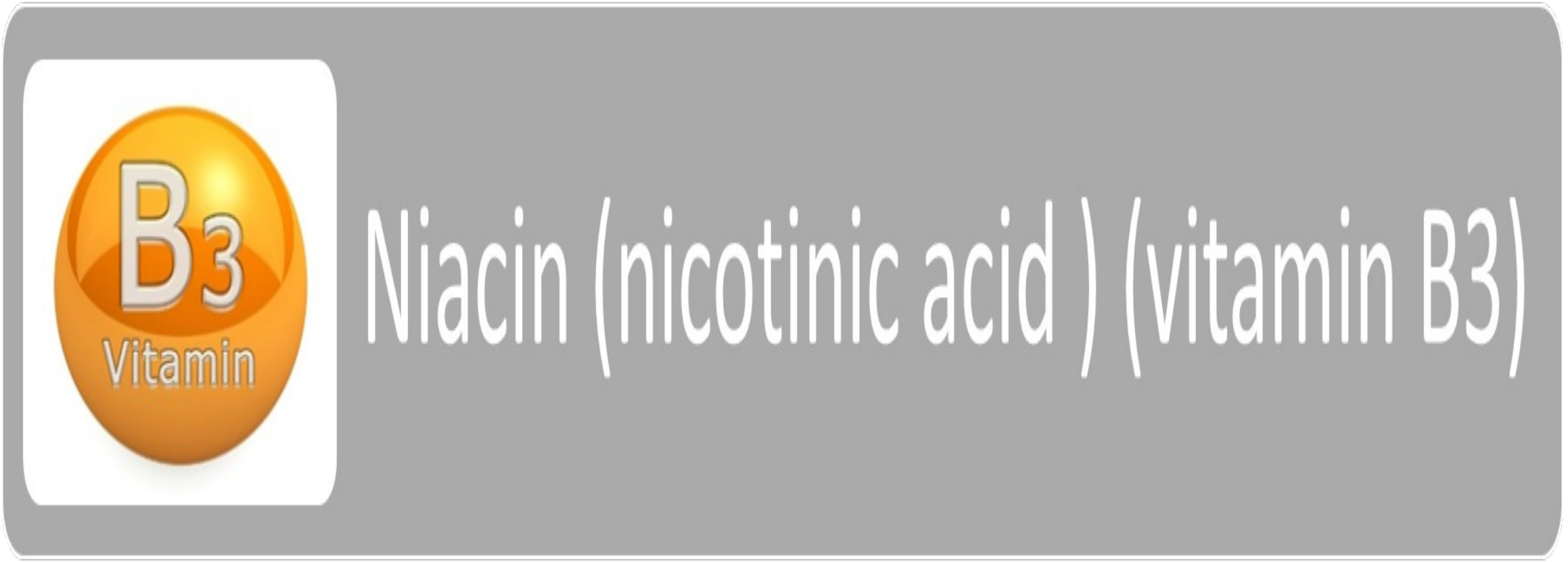
a. Vitamin B3

b. Vitamin B6

c. Vitamin B2

d. Vitamin C

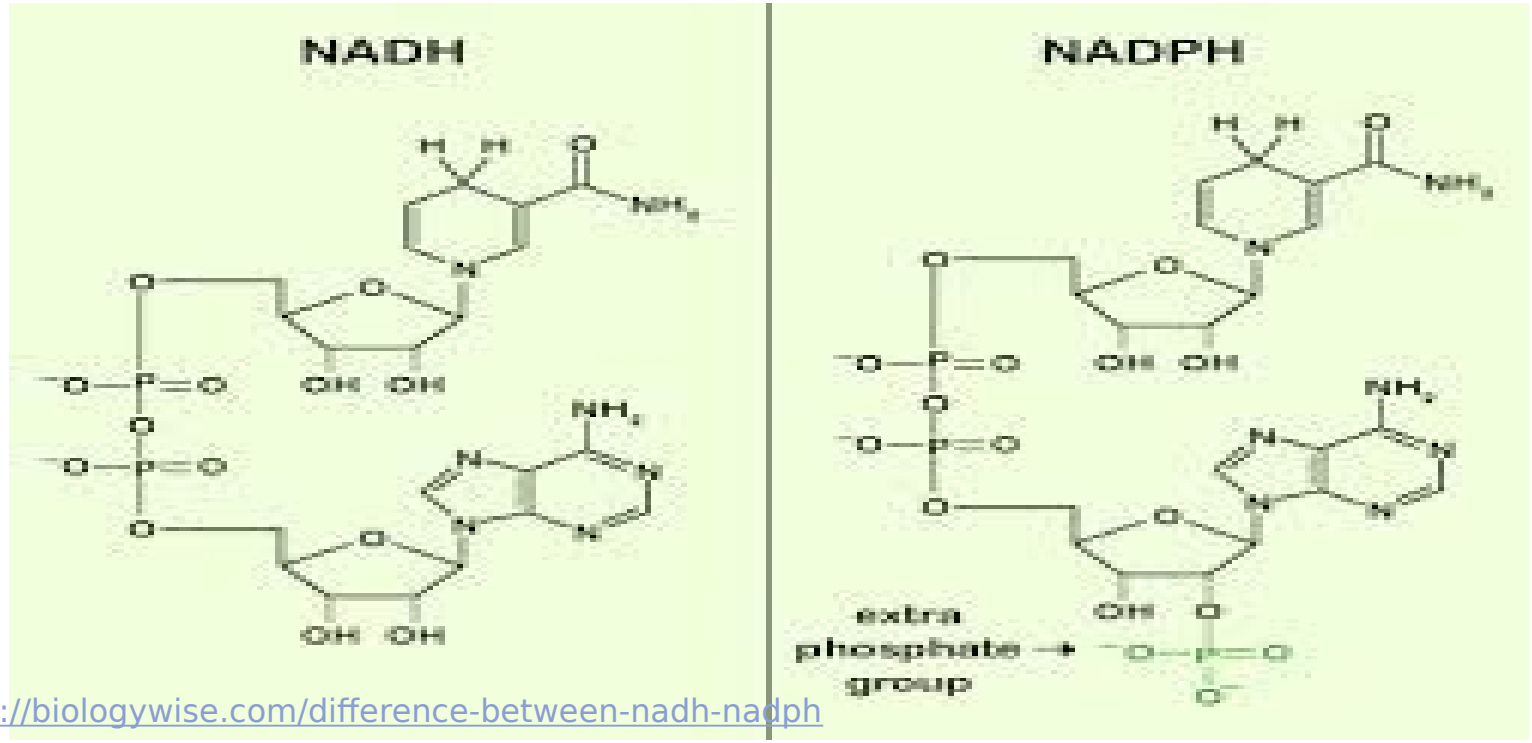
e. Vitamin D


B3
Vitamin
Niacin (nicotinic acid) (vitamin B3)

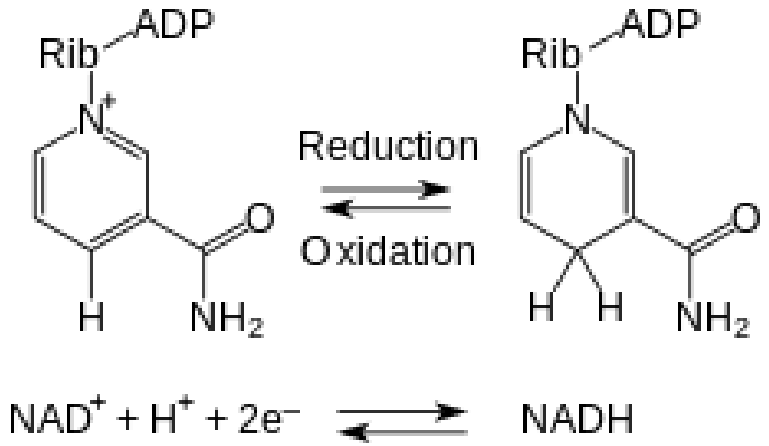
Niacin (nicotinic acid) (B_3)
Pellagra Preventive Factor (PPF)

Niacin is not strictly a vitamin since it can be synthesized from tryptophan (needs vitamin B6)

It is converted in the body into 2 hydrogen carriers (nicotinamide adenine dinucleotide **(NAD) &** nicotinamide adenine dinucleotide phosphate **(NADP)**



https://biologywise.com/difference-between-nadh-nadph



https://en.wikipedia.org/wiki/Nicotinamide_adenine_dinucleotide

NAD dependant enzymes

1. Glyceraldehydes 3-phosphate dehydrogenase
2. Lactate dehydrogenase
3. Pyruvate dehydrogenase complex
4. Mitochondrial isocitrate dehydrogenase.

NADP dependant enzymes

HMP

1. Glucose 6–phosphate dehydrogenase
2. 6-phosphogluconate dehydrogenase
3. Malic enzyme
4. Cytosolic isocitrate dehydrogenase
5. Glutathione reductase.

NADH generated is oxidized in the respiratory chain to generate 3ATP.

Niacin Deficiency (Pellagra)

Causes:

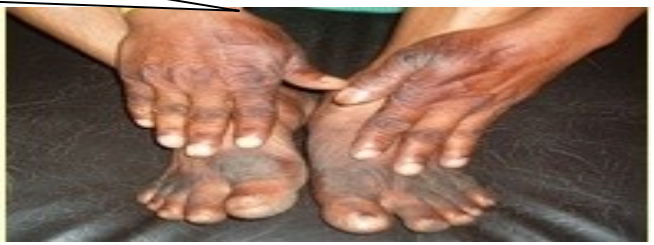
i. **Decrease Intake of Tryptophan & Niacin**

ii. **Vitamin B_6 deficiency (decreased conversion of Tryptophan to niacin)**

iii. **Caricinoid syndrome (shunting of tryptophan to serotonin synthesis)**

iv. **Hartnup's disease (decreased absorption of tryptophan): it is a Genetic condition in which there is a defect of the membrane transport mechanism for tryptophan resulting in large losses as a result of failure of renal reabsor**

Explain on biochemical basis pellagra manifestations in Hartnup's disease

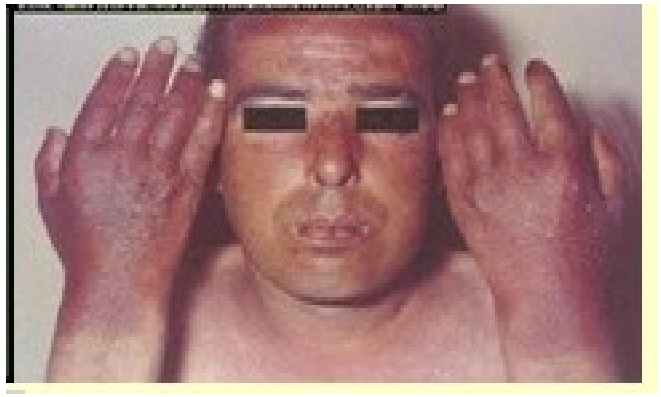


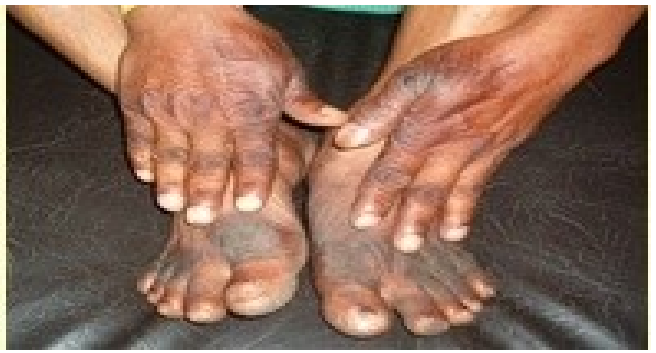
Manifestations: 3Ds

A.Dermatitis :rough scaly skin dark coloration of skin on the exposed parts of the body

B.Diarrhoea

C.Dementia: irritability, poor memory, peripheral neuritis and depression which end by dementia





Caricinoid tumour leads to deficiency of:

a. Vitamin B6

b. Vitamin B2

c. Vitamin C

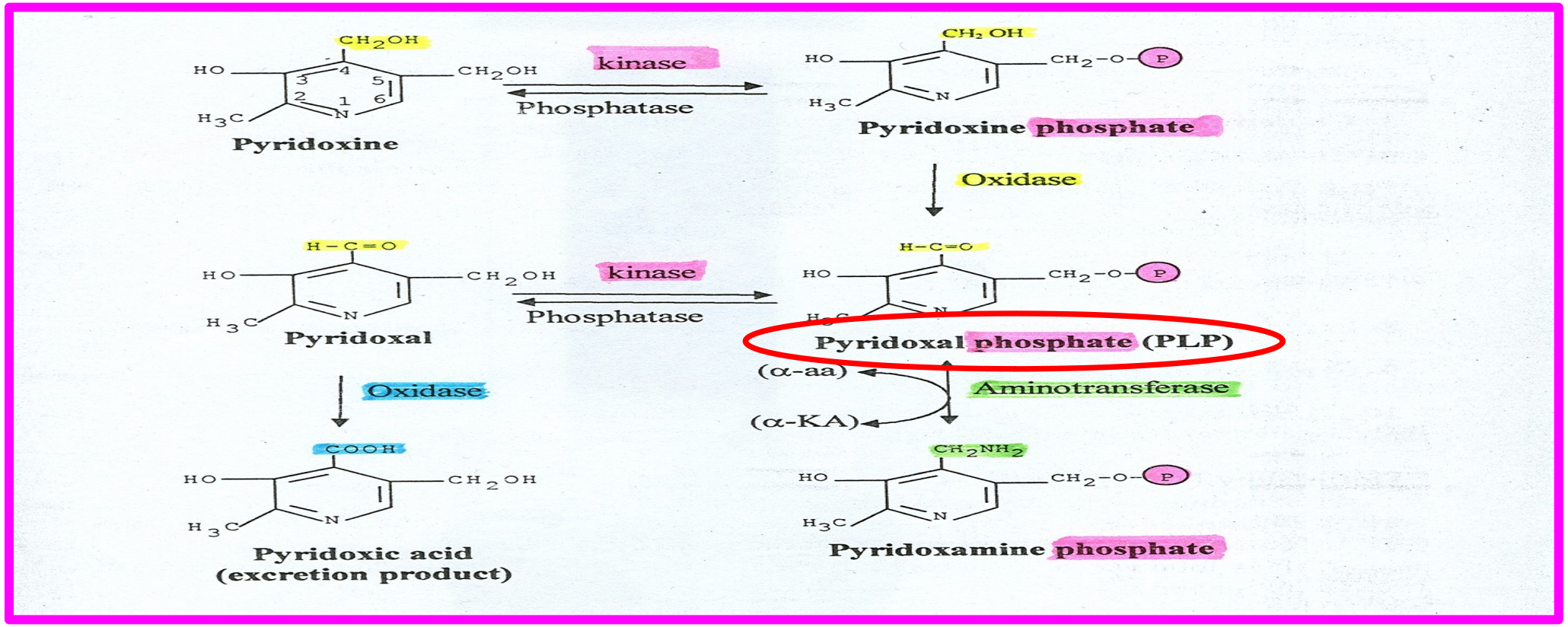
d. Vitamin B3

e. Vitamin D


B6
Vitamin
Pyridoxine (vitamin B6)

Pyridoxine vitamin (B6)

- **Active form of pyridoxine is pyridoxal phosphate (PLP).**



https://www.google.com.eg/url?sa=i&source=images&cd=&ved=2ahUKEwi2o8XmmPjjAhXBAGMBHUUrC30QjRx6BAgBEAQ&url=https%3A%2F%2Fwww.studyandexam.com%2Fvitamin-b6.html&psig=AOvVaw2pnBouGp1lCFjds1YiFeDd&ust=1565522713484423

Functions of PLP

A- acts as a coenzyme for many reactions in Protein metabolism:

1 - Absorption of amino acids and its uptake .

2- Transamination reactions e.g. ALT and AST.

3- All decarboxylation reactions of amino acids , e.g.

Explain on a biochemical basis

i- Glutamate ⟶ gamma amino butyric acid (GABA)

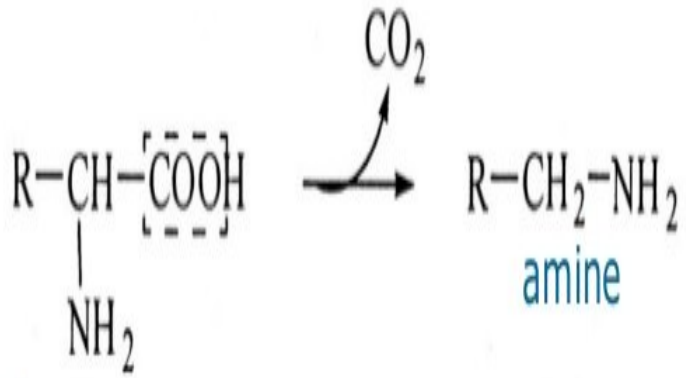
GABA is an inhibitory neurotransmitter, so in B_6 deficiency especially in children, epilepsy (convulsions) is common.

ii- Histidine ⟶ histamine

iii-5- Hydroxytrytophan ⟶ serotonin

iv- Cysteine ⟶ thioethanolamine and taurine

v- Serine ⟶ ethanolamine



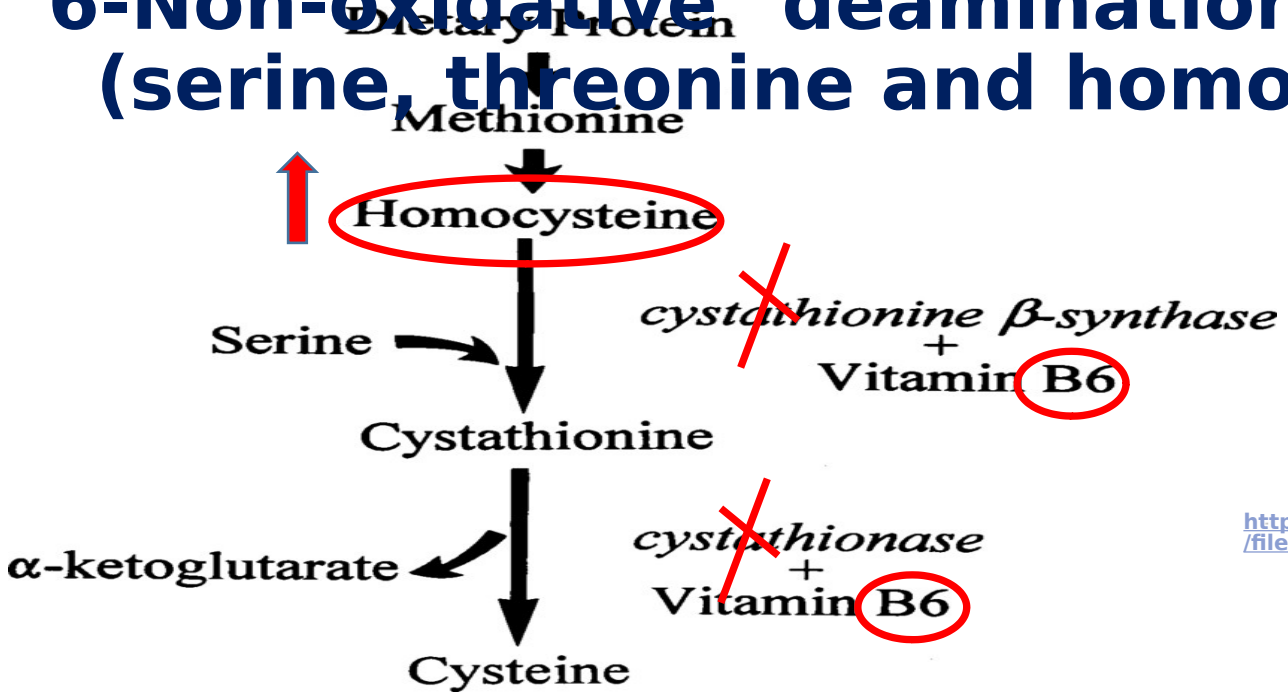
https://www.slideshare.net/senchiy/amino-acids-metabolism-new-12281450

4- Methionine and cysteine metabolism

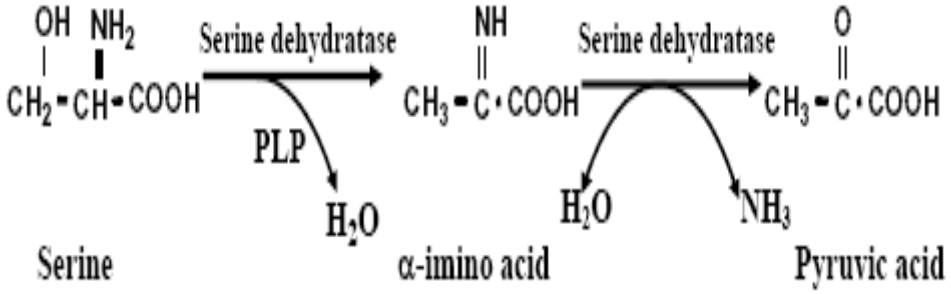
In vitamin B6 deficiency, (homocystinemia → hypertension

5-needed for conversion of tryptophan to niacin. So, in vitamin B6 deficiency pellagra like manifestations appear

6-Non-oxidative deamination of hydroxyamino acids (serine, threonine and homoserine)



https://www.researchgate.net/figure/Metabolic-pathway-for-the-conversion-of-methionine-to-cysteine_fig4_12732426



http://osp.mans.edu.eg/medbiochem_mi/Cources/Biochemistry/2nd_year_medicine/Protein_metabolism/files/Lecture_02.htm

B-In lipid metabolism: coenzyme in the formation of sphingosine from palmitoyl-CoA and serine.

C- In heme biosynthesis: PLP acts as coenzyme for ALA synthase (key enzyme in heme biosynthesis). So, in B6 deficiency, anemia is common.

Explain on a biochemical basis

D- In carbohydrate metabolism:

Muscle glycogen phosphorylase has a pyridoxal phosphate at each catalytic site.

Functions of PLP

Protein metabolism

1. absorption of amino acids and its uptake.
2. Transamination reactions e.g. ALT and AST.
3. decarboxylation reactions of amino acids
4. Methionine and cysteine metabolism
5. conversion of tryptophan to niacin.
6. Non-oxidative deamination .

Heme synthesis

4- **ALA synthase** in heme biosynthesis. So, in B6 deficiency, anemia is common.

Lipid metabolism

6- coenzyme in the formation of **sphingosine** from palmitoyl-CoA and serine.

Carbohydrate metabolism

Muscle glycogen-7 phosphorylase has a pyridoxal phosphate at each catalytic site

Deficiency of Vitamin B_6

Causes of deficiency:

- **Pregnancy**
- **Alcoholics**
- **Oral contraceptives & Penicillamine**
- **Tuberculous patient treated with isoniazid (explained later)**

Manifestations:

1-Hypochromic anemia due to impaired heme synthesis.

2-Neurological manifestations :

I.Peripheral neuritis (stock and glove) as PLP is involved in **sphingolipid synthesis**; so B_6 deficiency leads to demyelination of nerves.

II.Convulsions, particularly in children due to decreased formation of GABA.

3-Pellagra like manifestations due to decreased conversion of tryptophan to niacin.

4-Homocysteinemia and homocystinuria

Explain on a biochemical causes neurological manifestation in vitamin B6 deficiency?

Clinical indications for pyridoxine

- **Tuberculosis**
  - **Isoniazid, a drug commonly used to treat tuberculosis. It can induce vitamin B6 deficiency by forming an inactive derivative with PLP and inhibit endogenous synthesis.**
  - **Dietary supplementation with B6 is needed to prevent B6 deficiency caused by Isoniazid .**
- **Morning sickness (Nausea & vomiting in the first 3 months (trimester) of pregnancy:**

  Vitamin B6 is needed for protein metabolism and neurotransmitter metabolism as decarboxylation of dopa to dopamine, decarboxylation of glutamic to GABA.
- **Depression :**

  Through its role in creating neurotransmitters that regulate emotions, including serotonin, dopamine and gamma-aminobutyric acid

Explain on a biochemical basis

..... is essential for transamination reactions:

a. **TPP**

b. **CoASH**

c. **PLP**

d. **FAD**

e. **Biotin**

Key Points

- **Vitamins are essential; their deficiency may lead to a characteristic disease.**
- **FAD and FMN are the active forms of vitamin B2 (riboflavin). They act as hydrogen carriers.**
- **NAD+ & NADP+ are the active forms of vitamin B3 (Niacin). Its deficiency leads to pellagra.**
- **PLP, the active form of vitamin B6, acts as a coenzyme for many reactions especially in protein metabolism. Its deficiency may lead to anemia, neurological manifestations, and pellagra like manifestations.**

SUGGESTED TEXTBOOKS

- "Lippincott's Illustrated Reviews in Biochemistry" by P.C.Champe, R.A.Harvey and D.R.Ferrier
- "Harper's Biochemistry" by R.K.Murray, D.K.Granner, P.A. Mayes and V.W.Rodwell.
- Fundamentals of Clinical Chemistry (Tietz) Sixth
- "Textbook of Biochemistry with Clinical Correlations" by T.M.Devlin
- ***www.namrata.co- Biochemistry for medics***

Thank you